

Composition cosmétique ou pharmaceutique, notamment dermatologique, contenant un extrait de Vismia.**Publication number:** FR2700268**Publication date:** 1994-07-13**Inventor:** FREDERIC BONTE; ALAIN MEYBECK**Applicant:** LVMH RECH (FR)**Classification:****- international:** **A61K8/96; A61K8/00; A61K8/97; A61K36/00; A61K36/18; A61P17/00; A61Q19/00; A61Q19/08; A61K8/00; A61K8/96; A61K36/00; A61K36/18; A61P17/00; A61Q19/00; A61Q19/08; (IPC1-7): A61K35/78; A61K7/48****- European:** A61Q19/08; A61K8/97; A61K36/38**Application number:** FR19930000263 19930113**Priority number(s):** FR19930000263 19930113**Also published as:**WO9415626 (A1)
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CLAIMS

1 - Use of an extract of *Vismia* for the preparation of a composition cosmetic or pharmaceutical, in particular dermatological, stimulating the synthesis of collagen in particular, in particular that of collagen I, and intended in particular to fight against the effects of cutaneous ageing, to obtain a cutaneous hardening or to treat the various pathologies accompanied by a collagen deficiency.

2 - Use according to claim 1, characterized in that the above mentioned composition is intended to improve the cutaneous cicatrization.

3 - Use according to the claim 1 or 2, characterized in that the above mentioned extract is obtained starting from a plant of the *Vismia* kind chosen among the consistent group of *Vismia cayennensis*, *Vismia guianensis* (Aublet), *Vismia macrophylla* Kunth, *Vismia latifolia* (Aublet), *Vismia sandwithii* Ewans, *Vismia sessilifolia*, *Vismia guineensis*, *Vismia angusta*, *Vismia will confertiflora*, *Vismia amazonica*, *Vismia dealbata*, *Vismia ferruginea*, *Vismia tomentosa*, *Vismia will baccifera*, *Vismia* < RTI ID=10.1> *lindeniana*, < /RTI> *Vismia japurensis* < RTI ID=10.2> ; < /RTI> in particular starting from the barks or of the fruits of this plant.

4 - Use according to < RTI ID=10.3> One < /RTI> claims 1 to 3, characterized in that the above mentioned extract is obtained from *Vismia cayennensis*, of *Vismia amazonica* or *Vismia guianensis*.

5 - Use according to < RTI ID=10.4> One < /RTI> claims 1 to 4, characterized in that the extract of above mentioned *Vismia* is obtained by extraction by a polar solvent, such as methanol or a hydro-éthanolique mixture, preferably starting from the bark or of the fruits of the plant.

6 - Cosmetic composition, characterized in that it includes/understands, as active ingredient, a quantity cosmétiquement effective of an extract of *Vismia*.

7 - Composition cosmetic according to claim 6, characterized in that it is about a cosmetic composition stimulating the synthesis of collagen, in particular that of collagen I, and in particular intended to fight against the effects of cutaneous ageing, or to obtain a cutaneous hardening.

8 - Pharmaceutical composition, in particular dermatological, stimulating the synthesis of collagen, in particular that of collagen I, characterized in that it includes/understands, as active ingredient, a pharmaceutically effective quantity of an extract of *Vismia*.

▲ [top](#) 9 - Composition according to claim 8, characterized in that the aforementioned pharmaceutical composition is intended to improve the cicatrization or to treat the various pathologies accompanied by a collagen deficiency.

10 - Composition according to < RTI ID=11.1> One < /RTI> claims 6 to 9, characterized in that the concentration in extract of *Vismia* lies between 0,0001% and 1% in weight compared to the total weight of the final composition.

11 - Composition according to one of claims 6 to 10, characterized in that the above mentioned extract is obtained starting from a plant of the *Vismia* kind chosen among the consistent group of *Vismia cayennensis*, *Vismia guianensis* (Aublet), *Vismia macrophylla* Kunth, *Vismia* < RTI ID=11.2> *latifolia* < /RTI> (Aublet), *Vismia sandwithii* Ewans, *Vismia sessilifolia*, *Vismia guineensis*, *Vismia angusta*, *Vismia will confertiflora*, *Vismia amazonica*, *Vismia dealbata*, *Vismia ferruginea*, *Vismia tomentosa*, *Vismia will baccifera*, *Vismia lindeniana*, *Vismia japurensis* < RTI ID=11.3> x < /RTI> in particular starting from the barks or of the fruits of this plant.

12 - Composition according to one of claims 6 to 11, characterized in that the above mentioned extract is obtained from *Vismia cayennensis*, of *Vismia amazonica*, or *Vismia guianensis*.

13 - Composition according to one of claims 6 to 12, characterized in that the extract of above mentioned *Vismia* is obtained by extraction by a polar solvent, such as methanol or a hydro-éthanolique mixture, preferably starting from the bark or of the fruits of the plant.

14 - Composition according to one of claims 6 to 13, characterized in that the extract of above mentioned *Vismia* is selected among an extract methanolic of bark of *Vismia cayennensis* and fruit a hydro-éthanolique extract of *Vismia amazonica*.

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Composition cosmetic or pharmaceutical, in particular dermatological, containing an extract of Vismia.

The present invention relates to primarily a cosmetic or pharmaceutical composition, in particular dermatological, containing an extract of Vismia.

More precisely, the present invention relates to < RTI ID=1.1> the utili- < /RTI> sation of an extract of Vismia, for the preparation of a composition cosmetic or pharmaceutical, in particular dermatological, stimulating the synthesis of collagen in particular, and intended in particular to fight against the effects of cutaneous ageing, to obtain a cutaneous hardening, to improve the cicatrization or to treat the various pathologies accompanied by a collagen deficiency, as well as cosmetic compositions or < RTI ID=1.2> pharmaceu- < /RTI> ticks by comprising application.

The plants of the Vismia kind are known of long date in the Amazonian basin and Guyanes for their medicinal use, to look after the dermatoses as well as cutaneous eruptions, or like lacquer or sealing wax.

One knows in addition by the Journal document off

Natural Products, 1986, volume 49, < RTI ID=1.3> N < /RTI> 5, pages 929-931, the antitumor activity of the vismiones isolated from Vismia.

It was now discovered an activity surprising of the extracts of Vismia on the collagen synthesis, in particular of collagen of the type I, hereafter called in abbreviation ?collagenous I?, which makes them particularly useful to fight against the effects of cutaneous ageing, like obtaining a cutaneous hardening, or improving the cicatrization.

The purpose of the present invention is thus principal to solve the new consistent technical problem in the supply of a new formulation of a composition cosmetic or pharmaceutical, in particular dermatological, having a good effectiveness on the prevention or the treatment of the effects of cutaneous ageing, like on the cutaneous hardening, or to improve the < RTI ID=1.4> icatrisation. < /RTI>

The purpose of the present invention is still principal to solve this new technical problem in a particularly simple way, not requiring obligatorily the insulation of an active substance particular or its synthesis, satisfactory and usable on an industrial scale, in particular in cosmetic or pharmaceutical industry.

Thus, according to a first aspect, the present invention relates to the use of an extract of Vismia, for the preparation of a composition cosmetic or pharmaceutical, in particular dermatological, stimulating the synthesis of collagen in particular, in particular that of collagen I, and intended in particular to fight against the effects of cutaneous ageing, to obtain a cutaneous hardening or to treat the various pathologies accompanied by a collagen deficiency.

According to an alternative of realization the above mentioned composition is intended to improve the cutaneous cicatrization.

▲ top According to an alternative of preferred realization, the above mentioned extract is obtained starting from a plant of the Vismia kind chosen among the consistent group of Vismia cayennensis, Vismia guianensis (Aublet), Vismia macrophylla Kunth, Vismia < RTI ID=2.1> latifolia < /RTI> (Aublet), Vismia sandwithii Ewans, Vismia sessilifolia, Vismia guineensis, Vismia angusta, Vismia will confertiflora, Vismia amazonica, Vismia dealbata, Vismia ferruginea, Vismia tomentosa, Vismia will baccifera, Vismia < RTI ID=2.2> lindeniana, < /RTI> Vismia japurensis; in particular starting from the barks or of the fruits of this plant.

According to an alternative of realization, the above mentioned extract is obtained starting from a plant of the kind Vismia cayennensis, Vismia amazonica or Vismia guianensis.

According to an alternative of particular realization, the extract of above mentioned Vismia is obtained by extraction by a polar solvent, such as methanol or a hydro-éthanolique mixture, preferably starting from the bark or of the fruits of the plant.

In particular, the extract of Vismia can be obtained according to the process describes hereafter as an indication, but by no means Restrictive.

One carries out a first extraction of the bark or fruits of the plant, by a polar solvent, advantageously selected among the group consisted: < RTI ID=3.1> water, < /RTI> alcohols comprising preferably from 1 to 4 carbon atoms, chlorinated solvents preferably comprising 1 to 2 carbon atoms, organic esters comprising preferably from 3 to 6 carbon < atoms; RTI ID=3.2> ; < /RTI> or of a mixed solvent containing an unspecified mixture of above mentioned solvents.

Still preferably, the solvent of first extraction is selected among the consistent group of < RTI ID=3.3> water, < /RTI> methanol, < RTI ID=3.4> ethanol, < /RTI> a methanol-water mixture or a ethanol-water mixture, chloroform, the dichlorométhane. Still preferably, it is about < RTI ID=3.5> water, < /RTI> methanol, of < RTI ID=3.6> The

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éthanol < RTI > or Their mixtures.

The report/ratio of the bark or the fruits with the agent of extraction is not critical and generally will lie between 1: 5 and 1: 20 parts in weight.

The extraction is generally carried out at temperatures ranging between the ambient temperature and the point of boiling of solvent used for the extraction.

Preferably, this first extraction is carried out with the backward flow under atmospheric pressure throughout one 2 to 4 h. Moreover, it is advantageously preceded by a cold maceration during 2 to 4 a.m. in solvent of extraction.

At the end of the extraction, the phase of solvent containing

The extract is filtered then concentrated and/or evaporated dry under reduced pressure. One thus obtains a first extracted gross from

Vismia according to the invention. This rough extract can be purified according to various well-known processes with the man of < RTI ID=3.7> the art. < RTI >

According to a second aspect, the present invention relates to also a cosmetic composition characterized in that it includes/understands, as active ingredient, a quantity cosmétiquement effective of an extract of Vismia.

According to an alternative of particular realization, this cosmetic composition stimulating the synthesis of collagen, in by < RTI ID=3.8> ticulier < RTI > that of collagen I, is in particular intended to fight against the effects of cutaneous ageing, or to obtain a raffer missement cutaneous. Such a composition, for example, can < RTI ID=4.1> avanta- < RTI > geusement to be used as composition to prevent < RTI ID=4.2> the appari- < RTI > tion of the wrinkles or to attenuate the depth of it.

According to a third aspect, the invention still relates to a pharmaceutical composition, in particular dermatological, stimulating the synthesis of collagen, in particular that of collagen I, characterized in that it includes/understands, as active ingredient, a pharmaceutically effective quantity of an extract of Vismia.

According to a particular mode of realization, the aforementioned composition is intended to improve the cicatrization or to treat the various pathologies accompanied by a collagen deficiency.

In < RTI ID=4.3> one < RTI > or the other of the preceding aspects, one will preferably use the extract of Vismia to a concentration ranging between 0,0001% and 1% in weight compared to the total weight of the final composition. This is particularly the case when

The extract is built-in in an excipient, conveys or cosmétiquement or pharmaceutically acceptable support to constitute a cosmetic or pharmaceutical composition.

Other goals, characteristics and advantages of < RTI ID=4.4> The inven- < RTI > tion will appear clearly with the reading of the explanatory description which will follow, made in reference to several examples only given as illustration and which would know consequently in no way of limiting the range of the invention.

In the examples, the percentages are expressed in weight, unless otherwise specified. In the case of the extracts, the quantities of those are expressed in dry weight.

Example 1

Preparation of an extract < RTI ID=4.5> méthanolique < RTI > of bark of Vismia < RTI ID=4.6> cayennensi < RTI > One takes barks of Vismia cayennensis dried that < RTI ID=4.7> One < RTI > crush finely. Then 100 G of the broyat are included in 900 < RTI ID=4.8> ml < RTI > of methanol. The whole is carried to boiling and is maintained at this temperature during 1 H, then one filters to eliminate the barks.

One carries out then an evaporation of solvent, for example in a rotatory evaporator under reduced pressure and one recovers a concentrated extract known as extracted < RTI ID=5.1> 11. < RTI >

Example 2

Preparation of fruit a hydro-éthanolique extract of Vismia < RTI ID=5.2> amazoni ca < RTI >

One proceeds as described to < RTI ID=5.3> the exemple < RTI > 1 if it is only

One uses fruits of Vismia amazonica and that the solvent is < RTI ID=5.4> unmélange < RTI > water-ethanol 30/70.

One can repeat the hot extraction until exhaustion.

One gathers the various extracts and one carries out < RTI ID=5.5> The éva- < RTI > poration as described with example 1 until obtaining a said dry extract extracts 12.

Example 3

Description of the activity of an extract < RTI ID=5.6> méthanolique < RTI > of bark of Vismia cayennensis prepared according to example 1, extracted < RTI ID=5.7> I1, < RTI > on the collagen synthesis by human fibroblasts

One carries out a taking away of fibrobaste on the skin of 60 years a white woman during a Face lift and one cuts the skin in fine strips that < RTI ID=5.8> one < RTI > place in a trypsin solution at 0,25% during one night at 40C. The épidermiques cells are detached then from the derm after scraping.

The strips of derm thus obtained are cut out in cubic fragments from approximately 1 mm on side, named explants. These explants are deposited on a film of semi place E 199 < RTI ID=5.9> GIBC < RTI > < RTI ID=5.10> supplé- < RTI > menté with 2 mm from L-glutamine and 10% of serum of foetal wish, at a rate of 20 explants per limps of culture 100 mms in diameter.

Limp are incubated with 370C and the wet atmosphere enriched in CO2 (5%). The semi place is renewed twice per week.

When the cells reach the junction around explants, the fibroblasts are extracted without taking explants, by the use of a mixture trypsin 0,1 < RTI ID=5.11> %-EDTA, < RTI > 0,02%, and the fibroblasts are reimplanted in a semi place of culture renou < RTI ID=6.1> velé. < RTI > Some limp are used as witnesses and receive semi place renewed without

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the product of the invention, the others limp are divided into two batches receiving the product of < respectively; RTI ID=6.2> in~< /RTI> vention with 10 < RTI ID=6.3> , ug/ml.< /RTI>

One lets incubate during 48 H in the absence or in the presence of the product of the invention to the concentration indicated.

After 48 H of incubation, one carries out a proportioning immunoenzymatic of the collagen I secreted by the fibroblasts in the supernatant, by a method similar to that described by FOX S.I. and < RTI ID=6.4> al< /RTI> in Anal. Biochem. (1980), 104, 205-214.

The results obtained by this method of proportioning are indexed in table I hereafter.

The significativity of the results is given by means of the test of Student, with $p < 0,05$.

TABLE I

EMI6.1

< tb> < SEP> Collagen < SEP> I < SEP> secreted < SEP> % < SEP> of < SEP> sti- < SEP> Signifi
< tb> Cultures < SEP> by < SEP> fibroblasts < SEP> mulation < SEP> cativity
< tb> < SEP> < RTI ID=6.5> (ng/10000< /RTI> < SEP> cellules/48 < SEP> H)
< tb> Culture < SEP> witness < SEP> 635,2 < SEP> + < SEP> 29,9 < SEP> O
< tb> without < SEP> product
< tb> Product < SEP> of
< tb> the invention < SEP> < RTI ID=6.6> I1< /RTI> < SEP> < RTI ID=6.7> * < /RTI> < SEP>
< tb> 10 < SEP> < RTI ID=6.8> , ug/ml< /RTI> < SEP> 1 < SEP> 306,4 < SEP> + < SEP> 38,4 < SEP> + < SEP>
105,7 < SEP> < RTI ID=6.9> < SEP> S< /RTI> < SEP>
< tb>

S = significant

In table I, one expressed the quantities of collagen < RTI ID=6.10> I< /RTI> secreted by the fibroblasts in < RTI ID=6.11> ng/10000< /RTI> cellules/48 h.

It will be observed, starting from table I, that the extract methanolic of *Vismia cayennensis* produced a significant activity of stimulation of the collagen I synthesis by the fibroblasts.

On this subject, Shuster and Al, in Br. J. Dermatol. (1975), 93, 639-643, having for title ?The off Influences age, and sex one skin thickness, skin collagen and density?, highlighted a reduction in the collagen contents of the skin between 15 and 93 years.

Moreover, collagen is at the base of the architecture of the derm, < RTI ID=7.1> from where < /RTI> interest of product able to exert an effect of stimulation of the collagen I synthesis.

Example 4

Description of the activity of an extract hydro-éthanolique of fruits of *Vismia amazonica*, prepared according to example 2, extracted < RTI ID=7.2> I2, < /RTI> on the synthesis of collagen by human fibroblasts

According to the methodology described with example 3, one uses

The fruit extract of *Vismia amazonica* obtained to example 2, extracted I2, instead of the extract of barks of *Vismia cayennensis* obtained to example 1, while the taking away of fibroblasts was carried out on the skin of 56 years a white woman also during a face lift, and this, with various noncytotoxic concentrations of extract mentioned in table < RTI ID=7.3> II< /RTI> < RTI ID=7.4> Ci-après.< /RTI>

The significativity is determined, as in the preceding example, by means of the test of Student, with $p < 0,05$.

TABLE < RTI ID=7.5> II< /RTI>

EMI7.1

< tb> < SEP> Collagen < SEP> I < SEP> secreted < SEP> % < SEP> of < SEP> sti- < SEP> Signifi
< tb> Cultures < SEP> by < SEP> fibroblasts < SEP> mulation < SEP> cativity
< tb> < SEP> < RTI ID=7.6> (ng/10000< /RTI> < SEP> cellules/48 < SEP> H)
< tb> Culture < SEP> witness < SEP> 430 < SEP> + < SEP> 40 < SEP> O
< tb> without < SEP> product
< tb> Product < SEP> of
< tb> The invention < SEP> < RTI ID=7.7> I2< /RTI> < SEP>
< tb> 1,25 < SEP> pg/ml < SEP> 508 < SEP> + < SEP> 60 < SEP> +18 < SEP> S
< tb> 5 < SEP> < RTI ID=7.8> , ug/ml< /RTI> < SEP> 543 < SEP> + < SEP> 56 < SEP> +26 < SEP> S
< tb> 12,5 < SEP> < RTI ID=7.9> , ug/ml< /RTI> < SEP> 540 < SEP> + < SEP> 59 < SEP> +26 < SEP> S
< tb>

One can thus note, starting from table < RTI ID=8.1> II, < /RTI> that the extracts by a hydro-éthanolique mixture of fruits of *Vismia* also produce a significant activity on the stimulation of the collagen I synthesis by the fibroblasts.

Thus, the extracts of *Vismia* can advantageously be used, thanks to their property of stimulation of the synthesis of collagen, like active agent, in compositions cosmé- ticks or pharmaceutical, in particular dermatological, such as previously definite.

Various formulations of cosmetic compositions are given < RTI ID=8.2> Ci-après< /RTI>

Example 5

Freezing of cutaneous massage hardening - Extract of bark of *Vismia* according to the invention

example 1 1.0,1 G - Ethanol 25 G -
Glycerin 2 G - < RTI ID=8.3> Propylèneglycol< /RTI> 2 G < RTI ID=8.4> - Carbopol
946# 1,25 g< /RTI> - Aqueous Excipient with conservative possibly
< RTI ID=8.5> scented q.s.p.< /RTI> 100,00 G

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Part of the aqueous excipient is used with the < RTI ID=8.6> Carbopol< /RTI> to separately prepare a gel, the other part of < RTI ID=8.7> the exci- < /RTI> pient aqueous is used to be mixed with the other components and freezing is added in the solution obtained in order to obtain a gelled composition forming the freezing of massage.

This composition of freezing of massage can be used three times per week for two months on the level of the bust.

Example 6

Lotion of care of the body for the cutaneous hardening - fruit Extract of Vismia according to the example 2.0,5 G < RTI ID=8.8> - Agent solubilizing (Cremophor RH 40% 2 g< /RTI> - Acid < RTI ID=9.1> hyaluronique< /RTI> 1 G -

Aqueous excipient containing a conservative éven < RTI ID=9.2> tuellement scents q.s.p. 100,00 g< /RTI>

The extract is first of all solubilized in the solubilizing agent, then is added in the aqueous excipient to which one adds Hyaluronic acid.

The Lotion obtained can be used by three weeks cure on the zones sensitive to the relaxation, such as the belly, the thighs.

Example 7

Emulsion anti-wrinkle - Extract of bark of Vismia cayennensis according to < RTI ID=9.3> Example 1 - 0,10 g< /RTI> - Emulsified Excipient scented q.s.p. 100,00 G

Example 8

Composition healing - Extract of bark of Vismia cayennensis according to

example 1 1.0,5 G < RTI ID=9.4> - Excipient emulsified, standard water in oil q.s.p. 100,00 g< /RTI>